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HP-CDPS, CE-CDPS and CDPS were analyzed for their *in vitro* effect on coagulation and their ability to activate platelets in an *in vitro* assay to detect possible crossreactivity with HIT (heparin-induced thrombocytopenia) antibodies. CE-CDPS was selected for further qPCR analyses, in order to investigate whether this compound directly influences the gene expression of IL-6 and aggrecan.
Results: The monosulphated cyclodextrins ME-CD-6-S and -3S failed to affect aggrecan synthesis and IL-6 secretion by the OA chondrocytes. Polysulphated cyclodextrins MA-CDPS, HP-CDPS, CE-CDPS and CDPS at 5 μg/ml concentrations, on the other hand, significantly induced aggrecan production and repressed IL-6 release by the chondrocytes in culture. Five μg/ml of CE-CDPS, in contrast to MA-CDPS, HP-CDPS and CDPS, did not significantly activate platelets and thus showed no potential to induce HIT thromboembolic accidents *in vivo*. Therefore, CE-CDPS was selected for further qPCR analyses. These analyses confirmed the anabolic and anti-catabolic profile of CE-CDPS.
Conclusions: CE-CDPS is a new, structurally adjusted sulphated β-cyclodextrin derivative with preserved chondroprotective capacity and a promising safety profile.

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REGION SPECIFIC CELLULARITY OF ARTICULAR CARTILAGE IN THE TIBIAL PLATEAU OF THE MATURE SPRAGUE-DAWLEY RAT

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Purpose: Despite the frequent use of the rat in models of osteoarthritis (OA), little has been reported regarding the normal cellularity of articular cartilage (AC) and how this varies regionally in the AC across the rat tibial plateau. In this descriptive study, we evaluated the regional and zonal-depth specific cellularity of AC in the rat tibial plateau in mature animals.
Methods: Tibial plateau from five male Sprague-Dawley rats approximately 12 months of age were collected. NIH guidelines for the care and use of animals were observed (n=10 specimens). Specimens were formalin fixed, decalcified with 10% EDTA, and paraffin embedded. Serial, 5 μm-thick, coronal sections of the posterior half of the tibial plateau were deparaffinized and stained with Hematoxylin and Eosin prior to examination under light microscopy. Region specific (periphery, central and midline) measures were determined by dividing each compartment (medial and lateral) into 3 equally spaced regions (Fig. 1). Depth specific measures (superficial: 0-25%, mid: 25-50% and deep: 50-100%) were determined by dividing the AC thickness into three zones from the surface to the tidemark. Chondrocytes with visible nuclei were counted in each sub-area for each compartment. The cellularity of the AC (chondrocyte number/AC area) was determined for each sub-area. Three slides were evaluated for each leg. Analysis of variance was used to compare mean cellularity across compartments (medial, lateral), regions (periphery, center, and midline) and zonal depths (superficial, mid, deep). Post-hoc pairwise comparisons were performed using Fisher's LSD procedure.
Results: The overall mean cellularity of the lateral compartment was 130% that of the medial compartment ($p=0.004$). Cellularity varied significantly by depth and region within both the medial and lateral compartments ($p<0.001$ for each; Figs. 2 & 3). In the medial compartment, the overall cellularity progressively decreased with increasing depth from the surface ($p<0.001$ for each comparison). Comparisons across regions found that the cellularity of the medial periphery was 180% that of the center and midline regions ($p<0.001$).
Similarly, in the lateral compartment cellularity decreased greatly with increasing zonal depth ($P<0.001$ for each comparison) with the cellularity of the deep zone only 36% that of the superficial zone. The cellularity of the lateral compartment was significantly different for each region ($p<0.02$) with the mean cellularity highest in the periphery and least in the center region.
Conclusions: Compartment, regional and depth specific variations in AC cellularity were observed in the tibial plateau of mature Sprague Dawley rats in this comprehensive evaluation. The lateral compartment had a higher cellularity than the medial compartment and in both compartments cellularity was the highest in the superficial zone and the periphery region. Since all animals in this study were of the same age it is not known if some of these variations in cellularity may have developed with aging. These observed variations in cellularity across the tibial plateau may cause regional variations in response to experimental interventions. Care should be exercised to compare similar locations across animals in experimental studies.

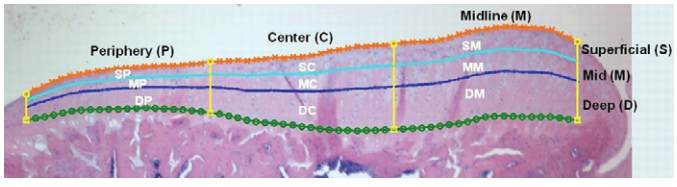

Figure 1. Articular cartilage of the tibial plateau illustrating the sub-areas evaluated in each compartment.

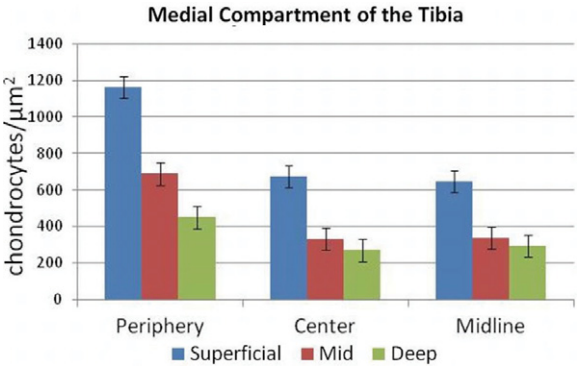

Figure 2. Articular cartilage cellularity of the medial compartment (mean±SE).

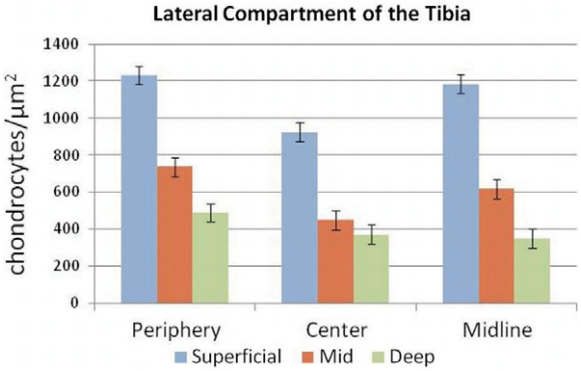

Figure 3. Articular cartilage cellularity of the lateral compartment (mean±SE).

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CHANGES IN THE ENDOPLASMIC RETICULUM AND GOLGI COMPLEX FROM CHONDROCYTES ARE RELATED WITH THE OSTEOARTHRITIS PATHOGENESIS

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Purpose. The aim of this study was to identify changes in the endoplasmic reticulum (ER) and Golgi complex (G) from chondrocytes of the three zones of the whole cartilage since early stages of Osteoarthritis (OA) pathogenesis.
Methods. The experimentally OA-induced model was accomplished by unilateral knee menisectomy and post-surgery training; normal rats were used as a control. Animals were sacrificed by CO2 overdose and right femoral condyles were removed and processed for either electron microscopy (EM) or Immunohistochemistry (IHC). Structural changes in the ER and G from chondrocytes were identified at 1, 2, 3, 4 and 5 training days (td) by EM. In addition, changes in the protein expression levels of ER (calnexin) and G markers (58-k9 protein) were evaluated by IHC at 5, 10, 20 and 45 td.
Results. During early stages of OA, chondrocytes undergo changes at morphological as well as at ultrastructural levels. These changes started in the superficial (SZ) and middle zones (MZ), showing a prominent ER development with expanded cisterns and enhanced G membranes. At the same time, chondrocytes acquired a rounded form and showed cells associations